Neurological manifestations in Covid-19 patients

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Game plan

- Review a couple of articles (including some case series) on neurological manifestations among Covid-19 survivors and decedents

Objectives

- Recognize that neurological complications from even mild cases can occur post recovery of acute infection, although neuro outcomes are more common in severe Covid-19 patients
- Describe some of the neurological abnormalities seen in Covid-19 cases
- Suggest studies that should be done moving forward

Take home messages

- SARS-CoV-2 effects more than just respiratory system, although compared to respiratory disease, neurological disorders are not as common
- Even among mildly ill Covid-19 patients, neurological abnormalities can be observed post recovery
- The sickest Covid-19 patients are more likely to develop neuro manifestations than those with milder illness, tho magnitude of risk is unknown/unmeasured at present (probably small)
- Although stroke is not common in Covid-19 patients, it needs to be recognized as a potential outcome, and if intervention can be effected, put into place

Introduction

- Most of the attention has been focused on respiratory disease and its complications
- Patients with Covid-19 develop a variety of neuro signs and symptoms
- Autopsy findings have shown brain edema and neuronal degeneration
- Rare isolation of SARS-CoV-2 in CSF—some experts cast doubt on this observation since it appears to be so infrequent
- In MIS-C patients discussed earlier, neurological symptoms and signs have been observed and can be the presenting symptoms and signs post recovery (or post community outbreak of Covid-19)

Common neuro symptoms/signs

- Headahe
- Seizures
- Disturbed consciousness
- Irritability
- Gait disturbance
- Acutely decreased smell (extremely common in some series)
- Acutely decreased taste (also commonly reported)

Coronaviruses in this genus can cause:

- Viral encephalitis (common in first SARS outbreak)
- Acute toxic encephalitis (which is reversible)
- Acute cerebrovascular disease, perhaps by cytokine storm

Potential mechanisms for neuro injury

- 1. direct infection or invasion of CNS
- Neuronal pathway from olfactory tract supports this mechanism, and animal models also support this (mouse models and rhesus models). Not much hard evidence in humans, like from autopsies.
- 2. hypoxia
- Causes cerebral edema and cerebral circulation disorders
- Hypoxia is a major feature of Covid-19

Mechanisms, continued

- 3. immune injury
- Linked to development of systemic inflammatory response syndrome
- Virus can infect macrophages, microglia, astrocytes (lab evidence to support this)
- "systemic hyper-inflammation provoked by an aberrantly excessive innate immune response'
- 4. ACE 2
- This enzyme is a protection factor for lots of organs, and also a target for SARS-CoV-2
- Binding increases BP, which increases stroke risk

Mechansims, cntd

- Both hypercoagulability and hypocoagulability have been suggested as stroke risks related to Covid-19

Chinese case series (n=214 patients in Wuhan)

- Mean age of Covid-19 patients 55 years
- 36% had neuro manifestations!
- Cognitive issues and stroke were not common, but observed

NYC stroke case series (n=5)

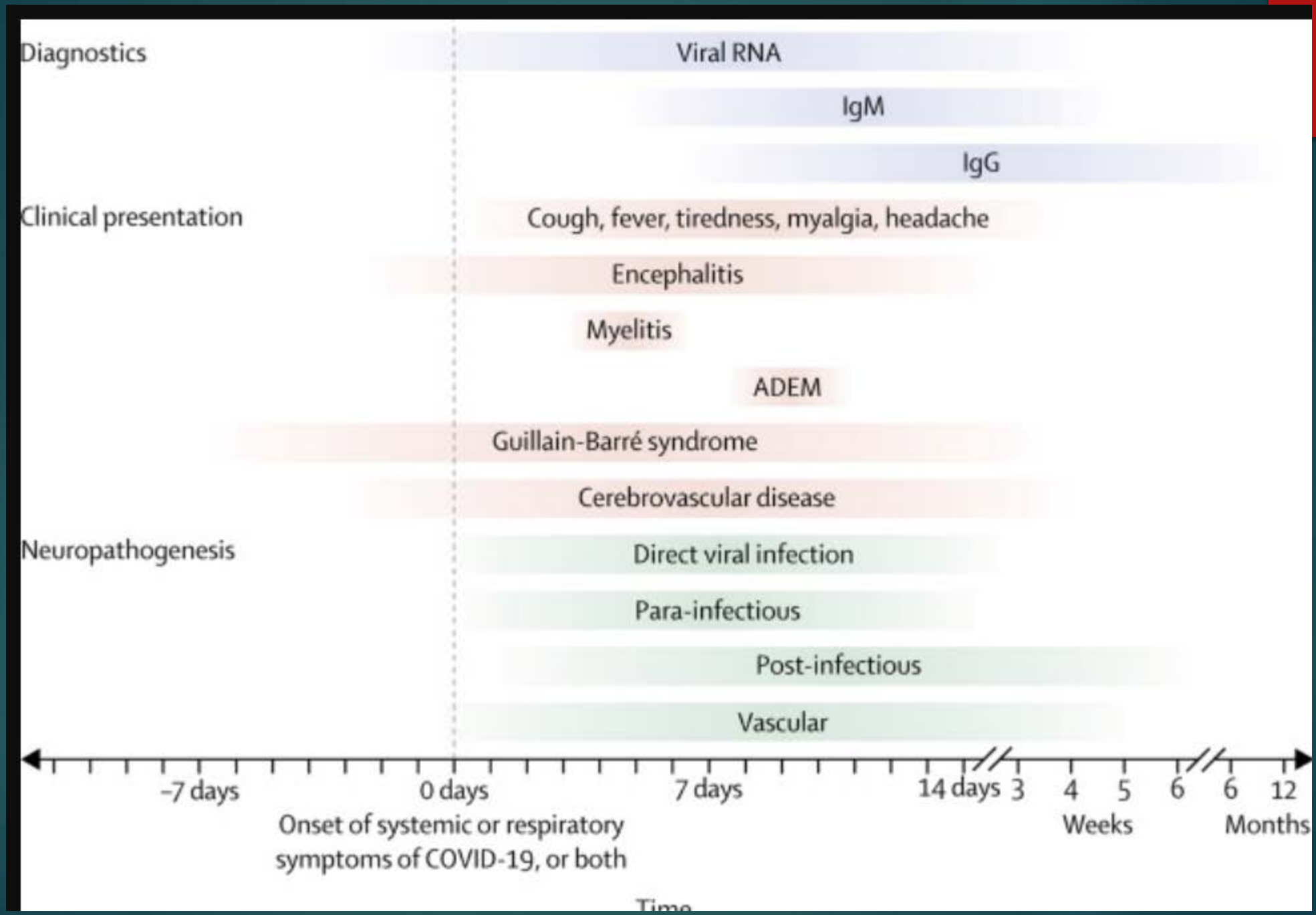
- All patients less than 50 years, all Covid-19 cases, entirely mild or no symptoms
- All five presented with large vessel ischemic stroke
- Etiologies unknown…hypercoagulable, arrhythmia, cardiomyopathy, dissection? Not much detail presented

- (Oxley, NEJM)

French case series (n=58 ICU patients with Covid-19)

- 84% had neuro signs
- 3 of 58 had ischemic stroke
- 7 had LP, with no pleomorphic cells or evidence of virus
- Scanning studies showed leptomeninges enhancement in 62%
- Perfusion abnormalities in 100%

- (Helms, NEJM)


Diagnostics
Viral RNA
IgM
IgG
Clinical presentation
Cough, fever, tiredness, myalgia, headache
Encephalitis
Myelitis
ADEM
Guillain-Barré syndrome
Cerebrovascular disease
Neuropathogenesis
Direct viral infection
Para-infectious
Post-infectious
Vascular
−7 days
0 days
7 days
14 days
3
4
5
6
6
12
Weeks
Months
Onset of systemic or respiratory symptoms of COVID-19, or both
Time

Looking ahead for effective interventions

- NIH is funding at least three clinical trials, evaluating effects of heparin or other anticoagulants on stroke prevention in Covid-19 patients
- If SARS-CoV-2 crosses blood-brain barrier, it will be important to develop therapies that have the capability of crossing the barrier to treat active viral infection

Recurrent themes, and moving forward

- Another area where there are more questions than answers
- Case reports and case series dominate the landscape
- If we knew more about pathogenesis, we might be able to do more re: prevention/intervention
- We need longer term follow up studies of a well-defined Covid-19 cohort, with different levels of disease severity, and including a panel of studies like: EEG, EMG, CT, LP, cognitive testing, etc.

References

- Wu et al, 2020
- Ellul et al, Lancet, July 2, 2020 This review highlights a number of case reports and case series, and, covers the waterfront with discussion of a variety of neurological diseases that have been associated with SARS-CoV-2 infections

- Thanks to Grazia Ori